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REVIEW ARTICLE - TUMOR - GLIOMA

Awake vs. asleep motor mapping for glioma resection: a systematic review and meta-analysis

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Abstract

Background Intraoperative stimulation (IS) mapping has become the preferred standard treatment for eloquent tumors as it permits a more accurate identification of functional areas, allowing surgeons to achieve higher extents of resection (EOR) and decrease postoperative morbidity. For lesions adjacent to the perirolandic area and descending motor tracts, mapping can be done with both awake craniotomy (AC) and under general anesthesia (GA).

Objective We aimed to determine which anesthetic protocol—AC vs. GA—provides better patient outcomes by comparing EOR and postoperative morbidity for surgeries using IS mapping in gliomas located near or in motor areas of the brain.

Methods A systematic literature search was carried out to identify relevant studies from 1983 to 2019. Seven databases were screened. A total of 2351 glioma patients from 17 studies were analyzed.

Results A random-effects meta-analysis revealed a trend towards a higher mean EOR in AC [90.1% (95% C.I. 85.8–93.8)] than with GA [81.7% (95% C.I. 72.4–89.7)] ($p = 0.06$). Neurological deficits were divided by timing and severity for analysis. There was no significant difference in early neurological deficits [20.9% (95% C.I. 4.1–45.0) vs. 25.4% (95% C.I. 13.6–39.2)] ($p = 0.74$), late neurological deficits [17.1% (95% C.I. 0.0–50.0) vs. 3.8% (95% C.I. 1.1–7.6)] ($p = 0.06$), or in non-severe [28.4% (95% C.I. 0.0–88.5) vs. 20.1% (95% C.I. 7.1–32.2)] ($p = 0.72$), and severe morbidity [2.6% (95% C.I. 0.0–15.5) vs. 4.5% (95% C.I. 1.1–9.6)] ($p = 0.89$) between patients who underwent AC versus GA, respectively.

Conclusion Mapping during resection of gliomas located in or near the perirolandic area and descending motor tracts can be safely carried out with both AC and GA.

Keywords Glioma surgery · Intraoperative stimulation · Awake surgery · Morbidity · Extent of resection · Motor mapping

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Alea Mohamed, Thannon Alsaeed, and Calder Prevatt are currently finishing their bachelor degrees.

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Abbreviations

IS	intraoperative stimulation
MSR	maximum safe resection
AC	awake craniotomy
GA	general anesthesia
EOR	extent of resection
STR	subtotal resection
GTR	gross total resection
LGG	low-grade glioma
HGG	high-grade glioma
RTC	randomized controlled trial
PFS	progression-free survival
OS	overall survival
C.I	confidence interval
MEP	motor evoked potentials
DTI	diffusion tensor imaging
iMRI	intraoperative magnetic resonance imaging

Introduction

Resective surgery has become the mainstay component for glioma treatment protocols [1, 8]. The most important objective for glioma surgery is obtaining maximum safe resection (MSR) of the lesion, which aims to achieve the highest extent of resection (EOR) possible with preservation of functional integrity. Greater EOR and favorable neurologic outcomes have been proven to positively impact patient prognosis by lengthening both progression-free survival (PFS) and overall survival (OS) [6, 7, 15, 26, 38].

Gliomas located in functional areas of the brain represent a challenging dilemma as aiming for greater EOR comes with an increased risk of permanent neurological deficit and potential worsening outcomes [26, 36]. To offer a surgical option to patients bearing an eloquent tumor, several technologies have been designed to provide safer methods of resection. Intraoperative stimulation (IS) mapping allows real-time and accurate identification of the cortical and subcortical eloquent areas as well as tumor-related epileptic foci [10, 14, 47]. IS mapping can be done awake or with general anesthesia (GA) for mapping motor and sensory cortices and the corticospinal tracts. This study aims to determine the effect of awake craniotomy (AC) vs. craniotomy under GA on the extent of resection (EOR) and postoperative neurological morbidity in gliomas located near motor areas of the brain.

Methods

This work was carried out according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [27, 28]. A focused question was developed with the PICO (Patient population, Intervention, Control, Outcome) criteria: Do patients with glioma lesions (patient population) in the perirolandic area or adjacent structures undergoing motor mapping with direct cortical stimulation (DCS) and AC surgery (intervention) have greater EOR and less neurological morbidity (outcome) when compared to surgery under general anesthesia (control). To adequately conduct and perform this study, the PRISMA checklist was utilized [28]. This study protocol was registered to the PROSPERO registry for systematic reviews.

Search strategy

Studies were identified by a medical librarian developing and running searches in the MEDLINE (1946–present), Embase (1974–present), Cochrane Central Register of Controlled Trials (1991–present), and the Cochrane Database of Systematic Review (2005–present) [all via the Ovid interface], Scopus (1823–present), Science Citation Index Expanded (1975–present), and Emerging Sources Citation Index (2015–present) [via the Web of Science interface] databases. Gray literature resources were also searched. There were no limits to language or publication date. Filters to remove animal studies, pediatric-focused literature, and certain publication types were used. The search strategies were created using a combination of keywords and standardized index terms. Search terms included MeSH, Embase/Emtree terms, as well as keywords such as “glioma”, “brain mapping”, “stimulation”, and “neurologic outcomes”. All databases and gray literature resources were searched on June 22, 2019. Full search strategy is available from the authors; search result data is reported in the supplementary figures (Table 1, Supplementary data).

Study selection

The study selection strategy was meticulously defined. Full-text articles written in English language, describing case series, observational studies, and clinical trials, were included. For inclusion, studies met the following criteria: patients with diagnosis of glioma in teen and adult patients; tumors located in or adjacent to the primary motor and/or primary sensory cortical areas or descending motor tracts; patients who underwent surgical resection of the tumor; motor mapping with direct cortical stimulation had to be carried out in all patients; articles evaluating neurological outcome of patients. We excluded publications written in other languages, case reports, basic science research, and review articles, articles with a population of $n < 20$, infratentorial tumors, studies including lesions other than gliomas, or if gliomas were not located in motor-related areas of the brain, more specifically, if they were located in other areas than in or near the perirolandic area or the corticospinal tracts. Studies conducting other types of interventions or publications involving language, visual, sensitive, or cognitive mapping were excluded. During phase 1, study titles were screened by two reviewers (P.S.M and L.M.H) independently. In phase 2, abstracts of studies selected during phase 1 were screened by the same reviewers. If neurological outcome was not mentioned in the abstracts, articles were excluded (Fig. 1). During the last phase, full-text studies were evaluated by four different authors (C.P., R.M., A.M., and T.A.), and double-checked independently by two different reviewers (P.S.M and L.M.H). Disagreements were resolved by consensus.

Data extraction and outcome measures

Data extraction was conducted following the DECiMAL guide [31]. It was carried out by four investigators (C.P., R.M., A.M., and T.A.), and all extracted data was cross-checked by two authors independently (P.S.M and L.M.H). Data was extracted using an Excel (Microsoft, Inc.) document specifically designed for this project. Discrepancies were

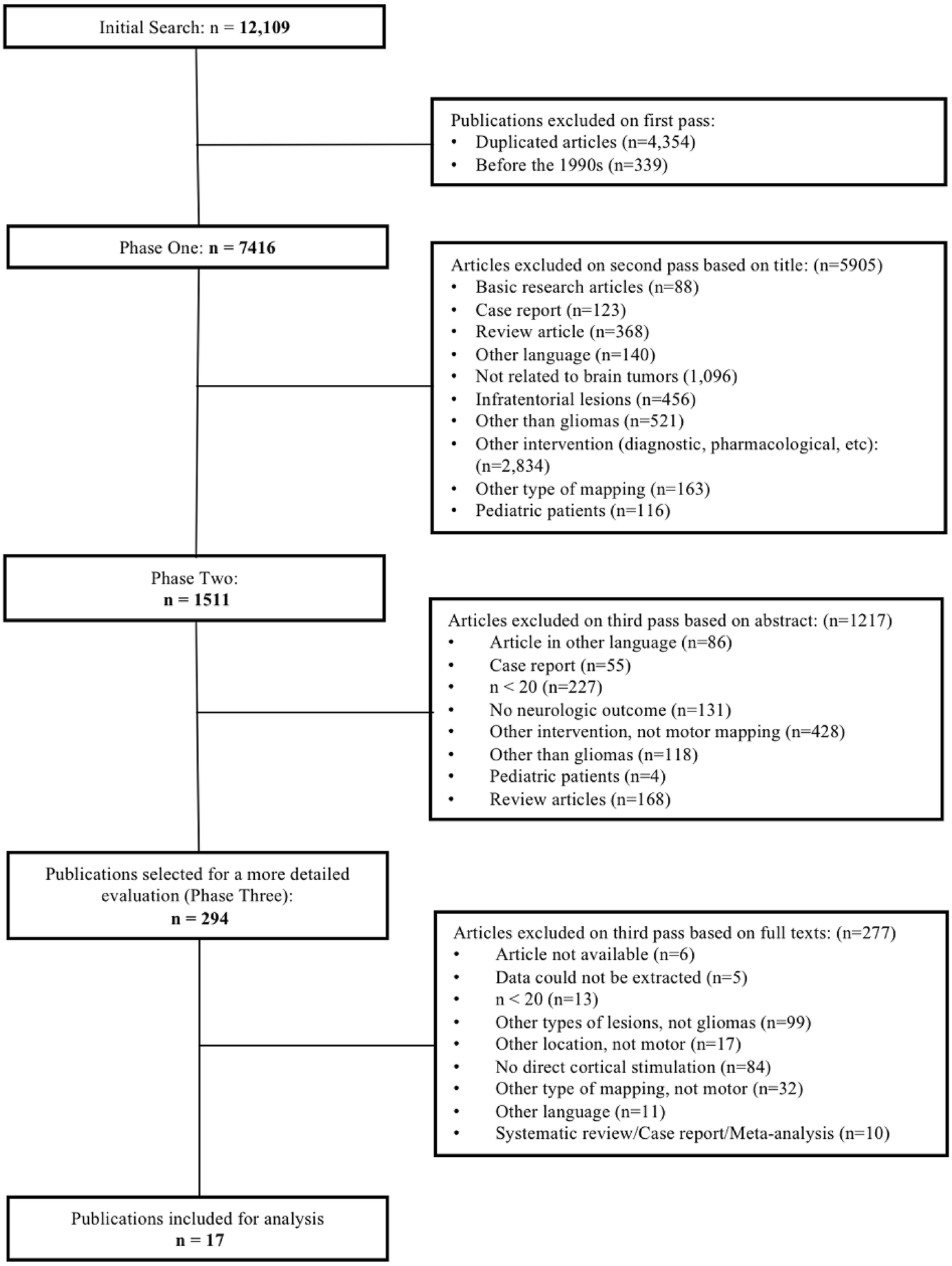

Fig. 1 Study selection flow chart

resolved by a third party or by consensus. The following variables from included articles were collected: author information, year of publication, study design, number and characteristics of patients, lesion characteristics, anesthetic protocol, motor mapping protocol, extent of resection, and neurological outcome of patients.

Primary outcome measures were EOR and postoperative neurological deficits. EOR was reported either quantitatively by mean volumetric measures or qualitatively divided by percentage of resection into three categories, i.e., partial resection, subtotal resection, and gross total resection (GTR), which were defined by a percentage of > 95% tumor resection or complete resection of contrast-enhancing lesions observed in postoperative imaging. Only articles reporting their results in a quantitatively manner were considered for statistical analysis. Neurological outcome was established with the scale used by De Witt Hamer et al [10]. Deficits were divided by timing in early/transient (< 3 months) and late/permanent (> 3 months) and by severity in severe (muscle strength grade 1–3 or vegetative state) and non-severe (all other types of motor neurological deficits). Articles including tumors in both motor and other areas of the brain, but motor mapping and postoperative neurological deficit information could be extracted separately were considered for analysis.

Quality assessment

All articles included in this work were first graded independently by two reviewers (P.S.M and L.M.H) and subsequently reviewed by the same authors in a consensus meeting using the Newcastle Ottawa Quality assessment tool [48]. Each article was evaluated for selection, comparability, and exposure. Studies with a score above 6 points were considered high quality. Disagreements were resolved by consensus (Table 2, Supplementary data).

Statistical analysis

Statistical analyses were conducted using R Studio, Version 1.1.383 (Boston, MA). The Meta-Analysis Package for R (metafor) version 2.0–0 was used to conduct the meta-analyses, tests for heterogeneity, and meta-regression. Weighted random-effects models were utilized to calculate a summary effect size for each outcome measure that was depicted on its corresponding forest plot with each pertinent study. The DerSimonian and Laird method was used to calculate between study variances. Given that these studies were performed over the course of several years and among differing populations, a random effects model was used over a fixed-effects model. Additionally, random-effects models are often preferred when the meta-analysis can be used to make patient care decisions. Heterogeneity was assessed using the I^2 statistic and the Cochran Q test. Significant heterogeneity was considered to be present if the I^2 statistic was > 50% and the p value of the Q test was < 0.10. Study arms were compared via meta-regression and Wald-type tests, where the null hypothesis was rejected for $p < 0.05$.

Results

Search results

The search initially yielded a total of 12,109 articles from seven different databases (Fig. 1). Duplicated studies were identified and deleted. Brain mapping in the field of neurooncology was first reported by Berger M.S. et al in the late 1980s [3, 4]. Only articles published after 1990s were included for analysis as the technique was better established by that time. After selection based on title and abstract, 294 studies underwent full-text eligibility assessment. Ultimately, 17 relevant studies were included for statistical analysis. All included studies were observational in nature and were published between the years 2004 and 2018.

Patient demographics and mapping characteristics

Patient characteristics of the analyzed studies are depicted in Table 1. A total of 2351 patients were included, of which 2329 underwent surgical resection with motor mapping. Included patients had an age range of 13–86 years, and 53.12% were male. All patients had the diagnosis of glioma within or adjacent to the perirolandic area or the descending motor tracts. A total of 46.61% of the lesions corresponded to low-grade gliomas (LGG), and 51.59% to high-grade gliomas (HGG), grading of the remaining gliomas was not specified. A total of 437 (18.58%) were operated with the AC protocol and 1892 (80.47%) patients had surgery under GA. Regarding mapping, 12/17 studies conducted both cortical and subcortical mapping; cortical mapping was only carried out in 2/17 and subcortical was only conducted in 3/17 studies. The detailed mapping characteristics of included studies can be found in Table 1.

Extent of resection

A total of 6/17 articles evaluated and reported the extent of glioma resection in a quantitative manner, reporting their results as mean percentage of EOR. Nine values of mean EOR were included in the meta-analysis (Table 2). The overall mean percent of EOR for patients undergoing IS mapping with awake surgery was 90.1% (95% CI: 85.8–93.8) whereas postoperative tumor volumes of patients under GA indicated an EOR of 81.7% (95% C.I: 72.4–89.7) ($p = 0.06$). This trended toward greater EOR in the AC as compared to the GA group, but did not reach statistical significance (Fig. 2).

Postoperative neurological deficits: timing

Sixteen prevalence estimates from 13 studies were included in the meta-analysis (Fig. 3). The overall random-effects pooled prevalence for early neurological deficits in patients undergoing IS mapping with AC was 20.9% (95% CI: 4.1–45.0%) versus GA with values of 25.4% (95% CI: 13.6–39.2%) ($p = 0.74$). For the overall analysis of late deficits, 15 prevalence estimates from 13 studies were considered. This analysis showed an overall pooled prevalence in late deficits of 17.1% (CI: 0.0–50.0%) for patients with AC and 3.8% (95% CI 1.1–7.6%) in patients operated under GA ($p = 0.06$). It is important to consider that for HGG, deficits can be present as a side effect of adjuvant treatment and/or related to disease progression. These results were, however, powered by one study [25].

Postoperative neurological deficit: severity

For deficit severity, 12 prevalence estimates originating from 10 studies were included (Fig. 4). The overall random-effects pooled prevalence indicated that patients undergoing mapping with AC had 28.4% (95% CI: 0.0–88.5%) of non-severe deficits whereas patients operated under GA had 20.1% (95% CI: 7.1–37.2%) ($p = 0.72$). Regarding severe deficits, the overall pooled prevalence of studies involving AC was 2.6% (95% CI: 0–15.5%), while studies involving GA had a pooled

Table 1 Characteristics of included studies

Study	Study design	Study period	n number	Males (n)	Glioma location	Histology (n)		Anesthesia protocol (n)		Mapping information		
						Low grade (n)	High grade (n)	GA (n)	AC (n)	Type of mapping	Type of electrode	Current applied
Keles E, et al. (2004) [20]	Retrospective Case Series	1987–2002	294	165	Within or adjacent to the motor cortex or its descending tracts ($n = 294$)	172	276	294		Subcortical	Bipolar	2-16 mA/60 Hz/1 msec
Kombos T, et al. (2009) [21]	Prospective Cohort	NA	40	28	Central Region ($n = 20$)		40	40		Cortical	Short train Monopolar pulses	5-25 mA/400-500 Hz/0.1–0.7 msec
Maesawa S, et al. (2010) [24]	Retrospective Case Series	2007–2008	28	17	Corticospinal tract ($n = 28$)	2	25	28		Corticosubcortical	Short train high-frequency grid electrode stimulator	10-30 mA/500 Hz/0.4 msec
Krieg SM, et al. (2012) [23]	Retrospective Case Series	2007–2010	112	62	Frontodorsal /anterior part of the internal capsule (32%), precentral gyrus (16%), postcentral gyrus (18%), pyramidal tract (34%)	20	92	112		Cortical	Strip electrode	6-30 mA/350 Hz/200–300 microsec
Ohue S, et al. (2012) [29]	Retrospective Case Series	2008–2009	32	17	Near the pyramidal tract ($n = 32$)	12	20	32		Corticosubcortical	Bipolar	12–20 mA/500 Hz/0.2 ms
Skrap M, et al (2012) [43]	Retrospective Case Series	2000–2010	66	40	Insular ($n = 66$)	53	13	33	33	Corticosubcortical	Bipolar	Cortical: 4 mA, Subcortical: 6-8 mA
Schucht P, et al (2013) [39]	Case Control Study	2007–2010	64	21	Central gliomas ($n = 33$), frontal lobe ($n = 31$)		67	67		Corticosubcortical	Bipolar	2-8 mA/60 Hz/1 msec
Bello L, et al (2014) [2]	Retrospective Case Series	2007–2012	591	338	Corticospinal tract ($n = 591$)	423	168	591		Corticosubcortical	Bipolar	2-15 mA/60 Hz/0.5 msec
Schucht P, et al. (2014) [41]	Prospective cohort	2010–2014	67	NA	Primary motor cortex or CST tract ($n = 67$)	64			64	Corticosubcortical	Monopolar	2-15 mA/4.0 msec
Ohue S, et al. (2015)	Retrospective case series	2008–2013	49	34	Subcortical course of the pyramidal tract ($n = 49$)		49	49		Corticosubcortical	Monopolar or Bipolar	10-30 mA/500 Hz/200 microsec. Subcortical:

Table 1 (continued)

Study	Study design	Study period	*n* number	Males (*n*)	Glioma location	Histology (*n*)		Anesthesia protocol (*n*)		Mapping information		
[30]												Bipolar stimulator at 20 mA
Plans G, et al (2016) [34]	Retrospective case series	2009–2013	92	NA	Primary motor cortex, CST, or both ($n = 92$)	NA	NA	92		Corticosubcortical	Monopolar	20 mA/500 msec
Javadi et al. (2017) [19]	Prospective cohort	2008–2017	20		Adjacent to the CST ($n = 20$)	6	14	20		Subcortical	Monopolar ($n = 8$) Bipolar ($n = 12$)	5-20 mA/500 Hz ($n = 8$), 50 Hz ($n = 12$)
Eseonu CI, et al. (2017) [13]	Retrospective Cohort	2005–2015	58	38	Peri-Rolandic ($n = 58$)	11	47	31	27	Corticosubcortical	Bipolar	2-8 mA/50 Hz/0.5 msec
Eseonu CI, et al. (2018) [12]	Retrospective case series	2005–2016	57	28	Peri-Rolandic ($n = 57$)	16	41		57	Corticosubcortical	Bipolar	4-10 mA/50 Hz/0.5 msec
Han SJ, et al (2018) [17]	Retrospective cohort	1997–2016	702	411	Peri-Rolandic ($n = 702$)	276	426	484	192	Subcortical	Bipolar	AC: 2-6 mA, GA: 4-16 mA/60 Hz/1 msec
Magill ST, et al. (2018) [25]	Retrospective cohort	1998–2016	49	27	Primary motor cortex ($n = 49$)	24	29	19	34	Corticosubcortical	Bipolar	AC: 1–6 mA, GA: 4-16 mA/60 Hz/1 msec
Saito T, et al. (2019) [37]	Retrospective cohort	2000–2018	30	23	Primary motor cortex ($n = 30$)	20	10		30	Corticosubcortical	Bipolar	2-6 mA/50 Hz/0.2 msec

Table 2 Included studies for quantitative EOR analysis

Study	Mean EOR awake craniotomy	Mean EOR general anesthesia	Difference between groups	Statistically significant?	Favoring
Skrap M (2012) [43]	83%	77%	$P = 0.001$	Yes	AC
Schucht P (2013) [39]	92.5%	–	–	–	–
Eseonu CI (2017) [13]	86.3%	79.6%	$P = 0.136$	No	–
Eseonu CI (2018) [12]	90.1%	–	–	–	
Magill ST (2018) [25]	90.8%	91.7%	$P = 0.83$	No	–
Saito T (2019) [37]	93%	–	–	–	–

prevalence of severe deficits of 4.5% (95% CI: 1.1–9.6%). There were no statistically significant differences in the prevalence of non-severe deficits ($P = 0.72$) or severe deficits ($p = 0.89$), between both groups.

Discussion

Mapping with IS has been proven as an effective surgical adjunct to maximize the EOR while preserving neurological function. This technique was first developed by Foerster and then refined by Penfield and Cushing in the early 1900s and, more recently, applied in the field of oncological neurosurgery to identify the relationship between neoplastic lesions and eloquent areas [3, 4, 20, 32, 33, 38]. IS mapping guides surgical resection by depolarizing a focal area of cortex simulating a deficit that one would obtain with surgical removal or activating a simplified version of normal sensorimotor behavior, which, if present, indicates the need to stop resection and preserve the responsive area.

IS mapping for motor and somatosensory areas can be performed under GA or an AC protocol [13, 22, 25, 45]. In the case of GA, motor function is monitored through electromyographic (EMG) recordings of the contralateral musculature. Whereas during an AC the patient is clinically evaluated and requested to indicate if there is muscle contraction or movement during cortical stimulation, looking for positive motor responses [34, 45]. Cortical stimulation with the patient awake also allows the surgeon to identify the most appropriate site for corticectomy. Moreover, while fully awake and cooperative, patients are asked to repeatedly perform a motor task to evaluate muscle strength and coordination during subcortical stimulation. This allows the surgeon to continuously identify positive motor responses and avoid damage to subcortical tracts, ensuring their integrity before resection. Furthermore, the AC carries the advantage that motor function can be tested

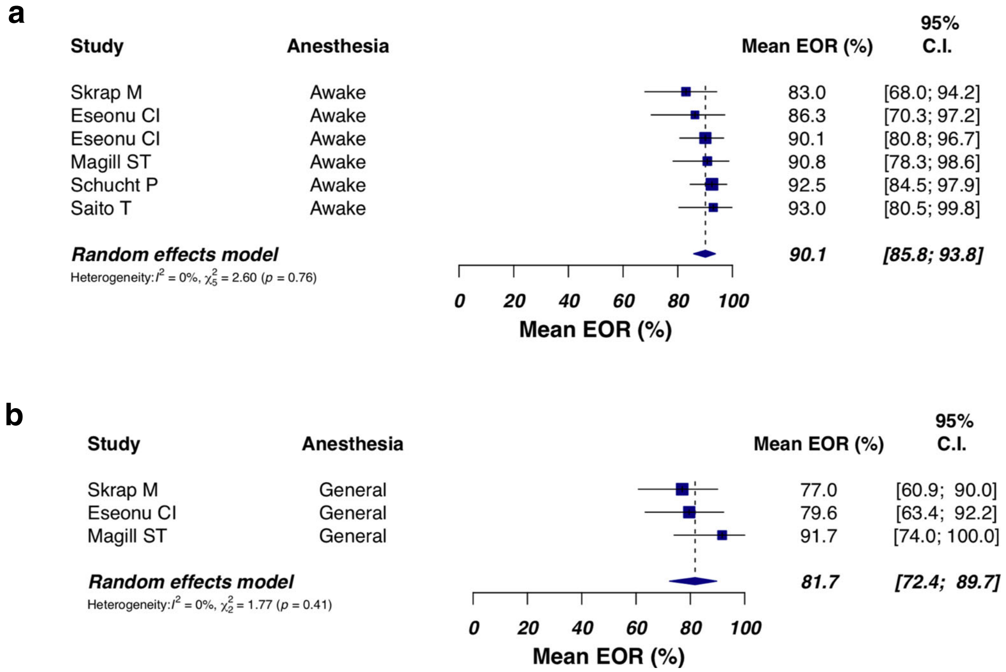

Fig. 2 **a** Awake craniotomy vs. **b** general anesthesia protocols in extent of resection (EOR) of gliomas located in motor cortex or adjacent areas

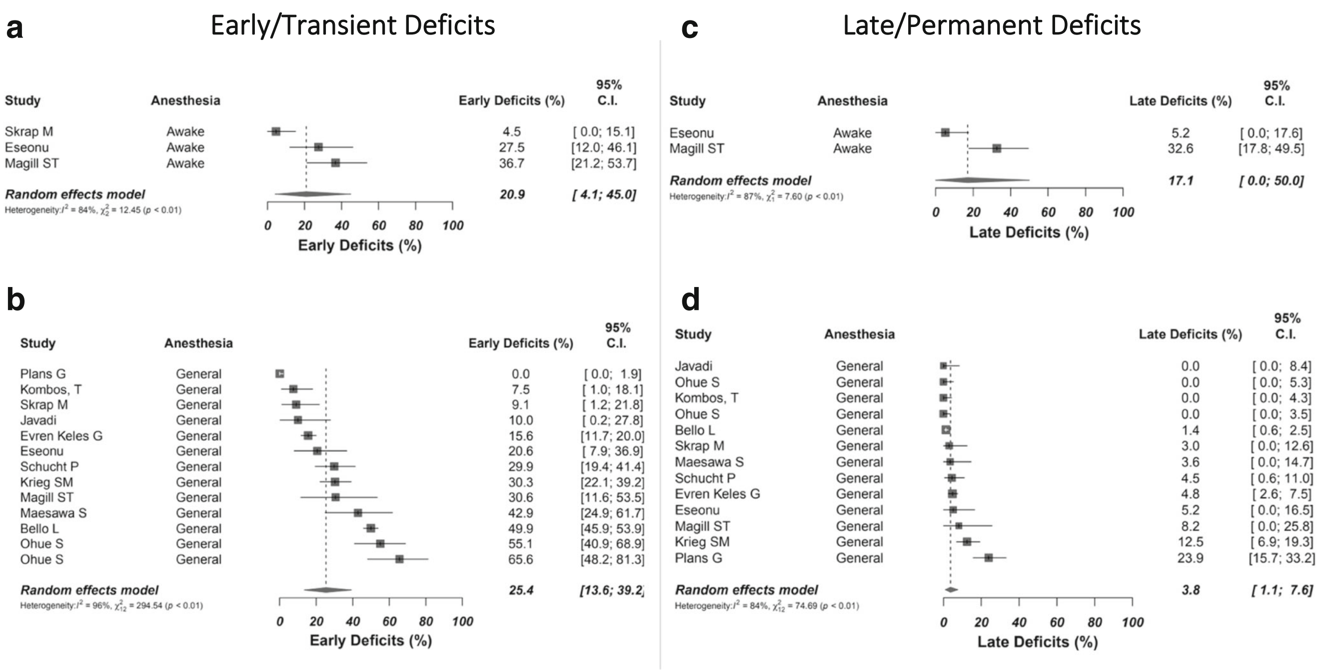

Fig. 3 Timing of neurological morbidity after resection of gliomas located in the motor strip. Early/transient deficits from **a** awake and **b** general anesthesia; as well as late/permanent neurological deficits in both **c** awake and **d** general anesthesia protocols are depicted here

while performing the active resection of the lesion. Because motor functions expand beyond mere muscle contraction and are thought to be a much more complex and integrated process, many proponents of an awake technique argue that tracking motor tasks throughout the surgery enables a safe, accurate, and more reliable manner of identifying eloquent motor cortex and subcortical motor tracts [25]. Its counterparts, however, criticize that pyramidal structures can be adequately detected and preserved under GA and that an awake protocol is related to higher rates of intraoperative seizures [45]. Prior studies have shown the benefit of IS mapping at improving the EOR and having increased favorable post-surgical outcomes; however, concerning motor-related gliomas, the current literature evaluating outcomes with these two techniques varies and high-quality evidence is not readily available.

To our knowledge, this study is the first meta-analysis comparing awake vs. asleep surgery and describing the postoperative outcomes of IS mapping specific to the motor cortex for

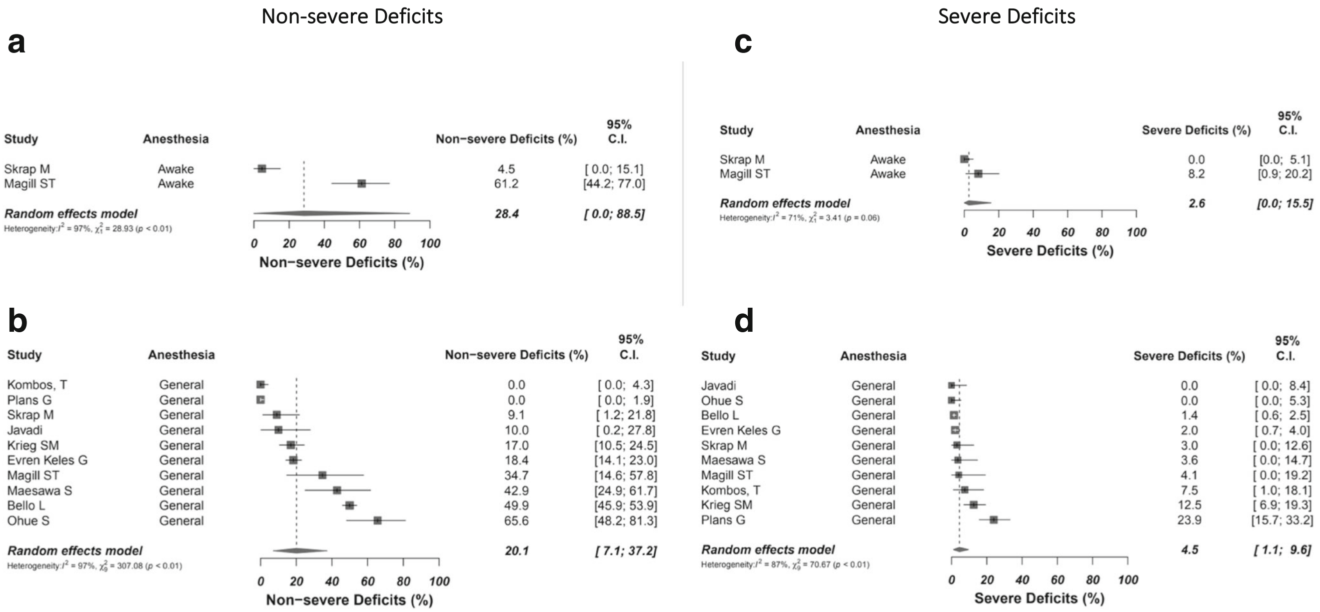

Fig. 4 Severity of neurological morbidity after resection of gliomas located in the motor strip. Non-severe deficits from **a** awake and **b** general anesthesia; as well as severe neurological deficits in both **c** awake and **d** general anesthesia protocols are depicted here

gliomas with these two anesthetic protocols. Our results suggest that this area has not been completely explored in order to be able to draw strong conclusions. Regarding EOR, there were no statistically significant differences between the two anesthetic protocols. Although a trend towards higher EOR was observed in studies with AC procedures, this trend agrees with previous literature which favors AC for achieving greater EOR in eloquent lesions [9, 16, 43]. Nonetheless, there is opposing evidence suggesting that there is no difference regarding EOR or postoperative tumor volumes between these two anesthetic modalities, but patients undergoing AC had more favorable overall outcomes [5, 13, 25, 47].

Postoperative motor deficits have been reported to vary between 4 and 17% for gliomas located in the perirolandic region [34]. Both the preoperative clinical baseline and the postoperative morbidity have been established as important prognostic factors [26]. In the meta-analysis conducted by De Witt Hammer et al., late severe neurological deficits were reduced when resective surgery was performed with IS mapping [10]. Regarding neurological deficits, our results show no differences between these two methods. From these data, we can conclude that performing IS for motor mapping under the AC protocol does not pose any additional risk of morbidity to patients when compared to GA or vice versa. For timing, our results showed a trend favoring AC in early neurological deficits. However, concerning permanent deficits, patients undergoing surgery with GA appear to have better long-term outcomes. Studies evaluating motor function predictors in perirolandic gliomas showed that positive subcortical mapping is directly related with greater long-term deficits [17, 34]. Moreover, Saito T. et al. established that intraoperative voluntary movement is significantly correlated with a decrease in long-term neurological morbidity, favoring the use of AC [37]. The data presented here are in accordance with previous published literature, reporting higher numbers of transient rather than late deficits with both anesthetic protocols. Theoretically, IS mapping provides a more reliable technique in preventing long-term neurological deficits. However, discharges during electrostimulation can temporarily inactive brain lesions with higher resolution; thus, it is often observed that patients who undergo IS mapping can have transient neurologic deficits that usually subside within the first 3 months after surgery [10]. Although AC had a higher pooled prevalence in late neurological deficits in this study, these were non-severe in nature. This trend on non-severe deficits is comparable to several rates of neurological impairment published elsewhere [39, 40, 42]. Whereas for resections carried under GA, our analysis showed higher numbers of severe deficits when compared to AC protocols. The observed trends on postoperative motor morbidity indicate that both of these techniques are safe for motor glioma resection and that neither anesthetic protocol significantly increases the percentage of postoperative motor morbidity when compared to each other.

Patients who undergo AC must be good candidates and fulfill specific requirements before being subjected to surgery [18]. One of the concerns with mapping gliomas related to the motor strip is the appearance of intraoperative seizures. A study conducted by Eseonu CI. et al evaluated a cohort of 57 patients who underwent an AC for motor-related gliomas and found a low incidence of seizures (8.8%) during the procedure, with a higher rate present in patients who exhibited positive mapping [12]. Another confounding factor to consider is the type of direct cortical stimulation; the 50 Hz or the train-of-five techniques play an important role in the incidence of intraoperative seizures due to the differences in frequency and length of stimulation. Although awake mapping is generally well tolerated, a small subset of patients can experience emotional distress during or after the procedure [44]. Patients who undergo awake mapping plus IS mapping are also subjected to longer anesthetic times. Therefore, surgery for functional tumor resection with awake mapping should be individualized and carefully planned according to the patient clinical status and the lesion characteristics.

Novel literature suggests that tumors located in or adjacent motor areas of the brain should not be considered inoperable [12, 17, 25]. Intrasurgical mapping enables real-time identification of critical structures. This is a significant advantage over other mapping techniques because of the inter-individual anatomic functional variations and the functional reorganization in cases of tumor recurrence [44, 49]. This technique also allows the surgeon to perform gross total and supratotal resections, which aims to remove greater volumes than the preoperative imaging signal abnormalities [11, 46]. Nonetheless, due to the need of adequate exposure, IS mapping is not compatible with minimally invasive procedures. With the use of intraoperative mapping, as well as other surgical adjuncts, resection with acceptable morbidity rates is now possible [10]. Several surgical devices have been and continue to be developed to grant a more precise identification of eloquent motor areas. In addition to IS mapping, the concomitant use of continuous monitoring of motor evoked potentials (MEP) has demonstrated to increase safety during resection of motor gliomas [21, 23, 34, 36]. IS mapping can also benefit from the use of diffusion tensor imaging (DTI)-based tractography, intraoperative magnetic resonance imaging (iMRI), and other novel technologies to better localize neoplastic tissue [19, 29, 30 39]. A new technique for motor mapping was published in 2014 by Raabe A et al. describing a continuous and dynamic IS with the objective of accurately determining the distance between lesions and motor tracts [35]. In this work, the authors were able to continuously stimulate the corticospinal tracts under general anesthesia with successful tumor resections and no permanent motor deficits related to this type of IS mapping [35]. The latter could represent a good and safe mapping alternative for patients that are not good candidates for awake surgery.

Study strengths and limitations

The broad search that was conducted for this study can assure that all articles related to glioma patients undergoing IS mapping for tumor resection were evaluated. Moreover, authors were very strict while analyzing all studies, and articles that did not meet all the inclusion criteria were immediately excluded from the analysis. On the other hand, the evidence found in the literature has a high risk of bias (Table 2, Supplementary data). Motor mapping with intraoperative stimulation has not been evaluated in randomized clinical trials (RCT). Most of the publications were observational and retrospective in nature; thus, conclusions drawn from this study must be interpreted with this in mind (Table 1). Due to the way tumor grading is reported in the included articles, we could not divide resections into low- and high-grade gliomas for sub-analysis. For the EOR results, it is important to consider that there could be variability between studies in the radiological measurements of resections. Moreover, EOR was reported differently as either STR, GTR (12/18 articles), or mean EOR (6/18 articles). Because of the differences in reporting their results, only studies reporting the mean EOR quantitatively were included for analysis. Similarly, postoperative neurological deficits were reported in different ways, and authors aimed to homogenize the data for posterior analysis.

Conclusion

Resection of gliomas located near or in the motor areas of the brain can be safely carried out with either GA of AC protocols. The results presented herein suggest that both techniques could be useful for motor mapping and glioma resection as neither of them appear to significantly pose a higher risk for patients when compared to the other. This topic is still on its early stages of investigation. However, it is important to consider the observed trends. Awakening the patient may allow a better EOR without significantly increase the risk of postoperative morbidity. This type of surgery should be carried out with caution, in the presence of a multidisciplinary team, and with selected patients considered apt to sustain an awake procedure. Also, when patients are not good candidates for an awake protocol, our results suggest that resections of gliomas located in the motor areas of the brain could also be carried out safely under a GA. As this anesthetic protocol resulted in lower rates of long-term deficits with acceptable EOR, these results also call for the need to conduct prospective studies comparing AC versus GA surgery, to be able to make more scientifically robust conclusions.

Authors' contributions Conception and design of the study: PSM, LMH, KLC. Literature search: TB. Acquisition of data: PSM, LMH, RMF, AM, TA, CP. Statistical analysis: EJL. Interpretation of data: PSM, LMH, EJL, HRG. Manuscript preparation: PSM, LMH. Critically revising the manuscript: DS, EHM, PSB, AQH, KLC.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants performed by any of the authors.

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